REMARKS

The Final Office Action mailed May 6, 2002, has been received and reviewed. Claims 46 through 60 are currently pending in the application. Claims 46 through 60 stand finally rejected. However, Applicants herein cancel claims 47 and 50 without prejudice or disclaimer, and Applicants herein propose to amend claims 46, 48, 53, and 60. Applicants respectfully request reconsideration of the application in light of the remarks and proposed amendments set forth herein.

35 U.S.C. § 102 Rejections

Claims 46 through 60 stand finally rejected under 35 U.S.C. § 102(b) (hereinafter "Section 102(b)") as being anticipated by one of Kjornaes et al. (U.S. 4,713,248), Chen et al. (U.S. 5,558,879), or Bartoo et al. (U.S. 4,743,248). However, in order for a reference to anticipate a claim under Section 102(b) that references must expressly or inherently set forth each and every element recited in the claim. *Verdegaal Brothers v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Applicants respectfully submit that, in light of the amendments proposed herein, none of the three references cited in the Final Office Action teaches or shows the subject matter recited in any of claims 46 through 60 in as complete detail as is provided in the claims, and as a result, Applicants respectfully request that the rejections of claims 46 through 60 under Section 102(b) be withdrawn.

I. Rejection of Claims 46 Through 58 and 60 as Anticipated by Kjornaes et al.

Claims 46 through 58 and 60 are rejected in the Office Action under Section 102(b) as being anticipated by Kjornaes et al. However, Applicants respectfully note that claims 47 and 50 are herein cancelled, and Applicants respectfully request that the rejection of these claims under Section 102(b) in light of Kjornaes et al. be withdrawn. With respect to claims 46, 48 through 49, 51 through 58, and 60, Applicants respectfully submit that, in light of the amendments proposed herein, Kjornaes et al. fails to expressly or inherently teach each and every limitation included in any of these claims. Applicants, therefore, respectfully request that the rejection of claims 46, 48 through 49, 51 through 58, and 60 under Section 102(b) be withdrawn.

As they are proposed to be amended, claims 46, 48 through 49, 51 through 58, and 60 require a dosage form including a first membrane in contact with a formulation comprising a therapeutic agent and a second membrane positioned over an outside surface of the first membrane, wherein the second membrane is a semipermeable membrane and the first and second membranes are formed such that the first membrane exhibits a permeability responsive to changes in osmotic pressure. However, Applicants respectfully note that the teachings of Kjornaes et al. do not contemplate a dosage form including first and second membranes as defined in the rejected claims. Kjornaes et al. teaches formulations and methods for preparing a dosage form containing a plurality of individual controlled release units (*e.g.*, "tiny time pills") coated with an inner film and an optional outer film. Specifically, Kjornaes et al. teaches film formulations that allow the individual units to be compressed yet remain flowable relative to one another. Significantly, the inner film and optional outer film taught in Kjornaes et al. act as a "diffusion coating" that "gradually lets the active substance in the units pass through." (*Kjornaes et al.*, col. 2, 3, 8, and 9). Neither the inner film nor the optional outer film taught in Kjornaes et al. is capable of acting as a semipermeable membrane, and the teachings of Kjornaes et al. do not explicitly or inherently teach a dosage form including a semipermeable second membrane. Therefore, the teachings of Kjornaes et al. do not anticipate claims 46, 48 through 49, 51 through 58, and 60, and Applicants respectfully request that the rejection of these claims under Section 102(b) be withdrawn.

In addition, the inner film and the optional outer film taught in Kjornaes et al. are not formed such that that the inner film will exhibit a permeability responsive to changes in osmotic pressure. Applicants respectfully submit that Kjornaes et al. includes no teaching regarding a membrane having a permeability that is responsive to osmotic pressure. Moreover, Applicants respectfully submit that the inner film included in the individual units taught by Kjornaes et al. would not inherently exhibit a permeability responsive to changes in osmotic pressure. Regardless of whether the individual units described in Kjornaes et al. include an outer film, both the inner film and outer film must allow diffusion of material out from the individual units. As a result, even if the inner film of Kjornaes et al. was formed using hydrophobic and hydrophilic materials suitable for providing a membrane responsive to osmotic pressure, the hydrophilic material would elute out of the inner film

before the hydrophilic material had sufficient opportunity to impart an osmosensitive response to the permeability of the inner membrane. This is particularly true in the anticipated environment of use for a controlled release dosage form (*i.e.*, the lower gastrointestinal tract), where the osmotic activity is generally not sufficient to insolubilize suitable hydrophilic materials. Therefore, Applicants respectfully submit that Kjornaes et al. fails to anticipate a dosage form including first and second membranes, wherein the first and second membranes are formed such that the first membrane exhibits a permeability responsive to changes in osmotic pressure, and Applicants respectfully request that the rejection of claims 46, 48 through 49, 51 through 58, and 60 under Section 102(b) be withdrawn.

II. Rejection of Claims 46 Through 58 as Anticipated by Chen et al.

Claims 46 through 58 are rejected in the Office Action under Section 102(b) as being anticipated by Chen et al. However, Applicants respectfully note that claims 47 and 50 are herein cancelled, and Applicants respectfully request that the rejection of these claims under Section 102(b) in light of Chen et al. be withdrawn. With respect to claims 46, 48 through 49, and 51 through 58, Applicants respectfully submit that, in light of the amendments proposed herein, Chen et al. fails to expressly or inherently teach each and every limitation included in any of these claims. Therefore, Applicants submit that the teachings of Chen et al. fail to anticipate the subject matter recited in claims 46, 48 through 49, and 51 through 58, and Applicants respectfully request that the rejection of these claims under Section 102(b) be withdrawn.

Upon consideration of the proposed amendments, claims 46, 48 through 49, and 51 through 58 recite a dosage form including a first membrane in contact with a formulation comprising a therapeutic agent and a second membrane positioned over an outside surface of the first membrane, wherein the second membrane is a semipermeable membrane and the first and second membranes are formed such that the first membrane exhibits a permeability responsive to changes in osmotic pressure. As is true of Kjornaes et al., Applicants respectfully note that the teachings of Chen et al. do not contemplate a dosage form including first and second membranes as defined in the rejected claims. The purpose of the Chen et al. patent is to provide a dosage form that does not include a pre-formed passageway for the release of medicament but forms such a passageway after administration

to an environment of operation. (*Chen et al.*, col. 1 –3). The dosage form taught in Chen includes a first inner coating around a compressed core and a second outer coating around the first inner coating. The dosage form of Chen et al. is designed such that, after administration to the environment of use, hydrostatic pressure builds within the core of the dosage form until the first inner membrane physically fails, forming an exit passageway. (*Chen et al.*, column 3, lines 41-55). The first inner membrane taught in Chen et al., therefore, could only be characterized as responsive to changes in hydrostatic pressure (*i.e.*, the membrane fails once a threshold pressure is reached), not to changes is osmotic pressure, and Chen et al. makes no mention of a membrane providing a permeability responsive to changes in osmotic pressure. Moreover, Chen et al. fails to expressly or inherently teach a dosage form including a semipermeable membrane. Therefore, applicants respectfully submit that the teachings of Chen et al. fail to anticipate the dosage forms recited in claims 46, 48 through 49, and 51 through 58, as they are proposed to be amended, and Applicants respectfully request that the rejection of these claims under Section 102(b) be withdrawn.

Applicants further submit that the design of the dosage form taught in Chen et al. prevents the first inner membrane included therein from inherently functioning as a membrane having a permeability responsive to changes in osmotic pressure. Even if the first inner membrane taught in Chen et al. was formed using hydrophobic and hydrophilic materials suitable for providing a membrane exhibiting a permeability responsive to changes in osmotic pressure, the dosage form design taught in Chen et al. would not allow the hydrophilic substance included in the membrane to impart an osmoresponsive permeability. Because the second outer membrane of the dosage for taught in Chen et al. is an immediate release membrane designed to rapidly erode or dissolve after administration, the dosage for design of Chen et al. exposes the first inner membrane to the operational environment. Such exposure of the first inner membrane would allow the hydrophilic substance to elute out of the membrane before the hydrophilic substance had sufficient opportunity to act as an osmoresponsive component. This is particularly true in the anticipated environment of use for a controlled release dosage form (*i.e.*, the lower gastrointestinal tract), where the osmotic activity is generally insufficient to insolubilize suitable hydrophilic materials. Like the design of the individual units of Kjornaes et al., the design of the dosage form taught in Chen et al. does not

anticipate a dosage form having first and second membranes as defined in claims 46, 48 through 49, and 51 through 58, as they are proposed to be amended. Thus, Applicants respectfully request that the rejection of claims 46, 48 through 49, and 51 through 58 under Section 102(b) be withdrawn.

III. Rejection of Claims 46 Through 60 as Anticipated by Bartoo et al.

Claims 46 through 60 are rejected in the Office Action under Section 102(b) as being anticipated by Bartoo et al. However, Applicants respectfully note that claims 47 and 50 are herein cancelled, and Applicants respectfully request that and that the rejection of these claims under Section 102(b) in light of Chen et al. be withdrawn. With respect to claims 46, 48 through 49, and 51 through 60, which are now pending, Applicants respectfully submit that Bartoo et al. fails to expressly or inherently teach each and every limitation included in any of these claims. In particular, Bartoo et al. fails to explicitly or inherently teach a dosage form including first and second membranes wherein "the first and second membranes are formed such that the first membrane exhibits a permeability responsive to changes in osmotic pressure." It is asserted in the Office Action that Bartoo et al. teaches a dosage form comprising an inside wall and an outside wall and the that "inside wall comprises a polymeric formulation that is responsive to environmental changes such as pH." Applicants respectfully note, however, that the claims presently pending in this application do not require dosage forms that include an inside wall that is simply responsive to environmental changes or to changes in pH. The claims pending in the present application require dosage forms including a first membrane that exhibits a permeability responsive to changes in osmotic pressure, and Applicants respectfully submit that Bartoo et al. fails to explicitly or inherently teach a dosage form including such a membrane. Applicants further submit that because Bartoo et al. does not teach a dosage form including a first membrane exhibiting a permeability responsive to changes in osmotic pressure, the claims currently pending in the application, which require such a dosage form, can not read on the subject matter disclosed in that reference. Applicants respectfully submit, therefore, that Bartoo et al. fails to anticipate the subject matter recited in claims 46, 48 through 49, and 51 through 60, and Applicants respectfully request that the rejection of claims 46 through 60 under Section 102(b) be withdrawn.

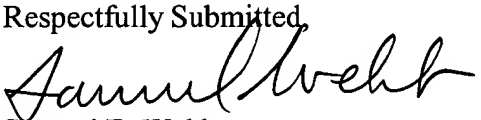
ENTRY OF AMENDMENTS

Applicants respectfully submit that entry of the proposed amendments to claims 46, 48, and 60 by the Examiner is proper. The Amendments are supported by the as-filed specification and drawings and do not add any new matter to the application. Further, the amendments do not raise new issues or require a further search. Finally, Applicants respectfully submit that the amendments proposed to claims 46, 48, and 60 place the case in condition for allowance. Therefore, Applicants respectfully request entry of the amendments proposed herein.

CONCLUSION

Claims 46, 48, 49, and 51 through 60 are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Examiner determine that additional issues remain which might be resolved by a telephone conference, he is respectfully invited to contact Applicants' undersigned attorney.

Respectfully Submitted,



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Enclosures: Version With Markings to Show Changes Made

SEW/eg

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

46. (Amended) A dosage form comprising:

a formulation comprising a therapeutic agent;

a first membrane in contact with said formulation[, the first membrane being formulated such that the permeability of the first membrane is responsive to changes in osmotic pressure]; and

a second membrane [in contact with] positioned over an outside surface of said first membrane, wherein the second membrane is a semipermeable membrane and the first and second membranes are formed such that the first membrane exhibits a permeability responsive to changes in osmotic pressure.

Please cancel claim 47 without prejudice or disclaimer

48. (Amended) The dosage form of claim 46, wherein said first and second membranes form an internal compartment containing the formulation.

49. The dosage form of claim 46, wherein the second membrane is formulated to maintain the integrity of the dosage form as the dosage form delivers the therapeutic agent.

Please cancel claim 50 without prejudice or disclaimer.

51. The dosage form of claim 46, wherein the integrity of the first membrane degrades during operation of the dosage form.

52. The dosage form of claim 46, wherein the first membrane comprises a hydrophilic substance and a hydrophobic substance.

53. (Amended) The dosage form of claim 52, wherein the hydrophilicity of the hydrophilic substance [is] changes in response to changes in osmotic pressure.

54. The dosage form of claim 46, wherein the first membrane is formulated such that the permeability of the first membrane increases in response to a decrease in osmotic pressure.

55. The dosage form of claim 46, wherein the formulation, the first membrane, and the second membrane are formulated and configured to deliver the therapeutic agent in an extended, non-declining release profile.

56. The dosage form of claim 55, wherein the extended, non-declining release profile comprises a period of about 30 minutes to about 24 hours.

57. The dosage form of claim 55, wherein the extended, non-declining release profile comprises a period of about 4 hours to about 24 hours.

58. The dosage form of claim 46, wherein the formulation, the first membrane, and the second membrane, are formulated and configured to deliver the therapeutic agent in a zero-order release profile.

59. The dosage form of claim 46, further comprising an expandable layer.

60. (Amended) A method of delivering a therapeutic agent to a subject, the method comprising:

administering a dosage form to the subject, the dosage form comprising a formulation including the therapeutic agent, a first membrane that is in contact with said formulation [and exhibits a permeability responsive to changes in osmotic pressure], and a second membrane [in contact with] positioned over an outside surface of said first membrane, wherein the second membrane is a semipermeable membrane and the first and second membranes are formed such that the first membrane exhibits a permeability responsive to changes in osmotic pressure.